Cataract in a Preterm Newborn: A Possible Side Effect of Linezolid Therapy

Eda İlarslan¹, Banu Aydin¹, Emrah Utku Kabatas², Serdar Beken¹, Dilek Dilli¹, Aysegul Zenciroglu¹ and Nurullah Okumus¹

ABSTRACT

Cataract may cause visual loss especially in the newborn period if early and urgent intervention is not managed. Approximately 1/3 of cases are congenital, 1/3 are related with systemic diseases and the remaining 1/3 are idiopathic or sporadic. The prevalence of congenital cataract in developed countries is estimated as 1 - 3 per 10,000 live births. There are a number of medicines besides systemic and infectious diseases which may cause cataract. Linezolid is a member of the oxazolidinone antibiotic family which can be used in serious infections caused by vancomycin resistant *E. faecium* (VRE), methicillin resistant *S. aureus* (MRSA), methicillin resistant coagulase negative staphylococci and penicillin resistant *S. pneumonia* in infants and children. Side effects are reported as diarrhea, vomiting, headache, transaminase elevation, rashes and optic neuropathy. Herein, we report a preterm newborn who developed thrombocytopenia and bilateral cataracts during linezolid therapy and relieved one week after the discontinuation of the therapy.


INTRODUCTION

Cataract is a disease characterized by opacification of the lens leading to impairment or loss of vision. Mainly corticosteroids as well as other medications such as allopurinol, potassium sparing diuretics and L-thyroxin administration in neonatal period have been reported to cause cataract. Linezolid is the first member of the oxazolidinone antibiotic family which can be used in serious infections caused by vancomycin resistant *E. faecium* (VRE), methicillin resistant *S. aureus* (MRSA), methicillin resistant coagulase negative staphylococci and penicillin resistant *S. pneumonia* in infants and children. Reversible thrombocytopenia developing after the second week of therapy as a side effect of linezolid is reported in children.

Herein, we report a preterm newborn who developed thrombocytopenia and bilateral cataracts during linezolid therapy and relieved after discontinuation of therapy.

CASE REPORT

A 840 g male infant, born to a 36 years old mother by caesarean section after 26 weeks of gestation, was admitted to Neonatal Intensive Care Unit (NICU). There was no consanguinity between parents and the mother was not diabetic. The patient was put on nasal Intermittent Mandatory Ventilation (IMV) support after the administration of prophylactic surfactant (200 mg/kg) in the delivery room. An empiric prophylactic therapy consisting of ampicillin and gentamicin and prophylactic dosage of fluconazole was initiated. Antibiotics were terminated after 10 days as negative blood culture result was examined. Screening examination for Retinopathy of Prematurity (ROP) at 31 weeks of corrected age revealed avascular zone 2. Retinopathy of prematurity and plus disease was not observed. The patient was diagnosed as late onset sepsis on day 40 because of apnea and fever. A combination of vancomycin and meropenem regimen was applied after blood and cerebrospinal fluid cultures were performed. Vancomycin Resistant Enterococcus (VRE) was isolated in the blood culture on day 47. Thereafter, vancomycin therapy was terminated and linezolid (10 mg/kg/day, twice daily) was started. On routine ROP examination, vacuoles located in the peripheral portion of the lens close to the posterior capsule (early stage of cataract) were observed on day 50, on the third day of linezolid treatment (Figure 1). The laboratory evaluation results regarding the etiology were as follows: Blood gas pH: 7.30, pCO₂: 60 mmHg, HCO₃: 29 mmol/L, Hb: 8.5 g/dl, Hct: %26.1, WBC: 6700/mm³, thrombocyte: 185,000/mm³, BUN: 7 mg/dL, creatinine: 0.25 mg/dL, glucose: 102 mg/dL, Na: 138 mEq/L, K: 4 meq/L, Cl: 102 meq/L, calcium: 8.5 mg/dl, phosphorus: 4.7 mg/dl, ALP: 185,000/mm³, BUN: 7 mg/dL, creatinine: 0.25 mg/dL, glucose: 102 mg/dL, Na: 138 mEq/L, K: 4 meq/L, Cl: 102 meq/L, calcium: 8.5 mg/dl, phosphorus: 4.7 mg/dl, ALP: 500 IU/L, AST: 46 IU/L, ALT: 17 UL/L, total/direct bilirubin: 0.4/0.3 mg/dL, 25 OH D vit: 27.5 mcg/L, normal parathormone level and negative reductant material and sugar chromatography in urine. Anti-CMV Ig G-M, anti-Rubella Ig G-M, anti-toxoplasmosis Ig G-M, anti-HSV Type 2 Ig G-M ve VDRL levels resulted as negative.

Cataract was also evident on the eye examination performed on day 13 of linezolid therapy. The thrombocyte levels were within normal ranges before the antibiotic therapy and gradually decreased to 52,000/mm³ and 34,000/mm³ in the follow-up.
Enteral feeding was initiated, acute phase reactant levels returned to normal and negative repeated blood culture results were obtained on day 18 of therapy and thereafter it was discontinued. It was observed 2 days later that thrombocyte levels returned to 112,000/mm³ without any transfusion and regression in cataracts was shown in the eye examination at the same time. There was no sign of cataract in the eye examination one week later (Figure 2). It was proposed to be related with linezolid therapy. While repeated ROP examinations were handled, laser photocoagulation was applied to the patient on day 78 because of bilaterally aggressive zone 2 ROP. The patient whose clinical general situation, activity and enteral feeding achieved fine with normal ophthalmological findings, was discharged on day 118.

**DISCUSSION**

Cataract is a condition characterized as progressive loss of transparency of the lens. Patients diagnosed in the first 12 months are named as infantile cataract whereas cases present at birth or diagnosed in the first month of life are defined as congenital cataract. In this case, cataract is very essential. Craniofacial syndromes, metabolic diseases (galactosemia, hypoparathyroidism, infantile hypoglycemia, maternal diabetes, mannosidosis, Fabry disease, Refsum disease, Zellweger syndrome), skeletal system diseases (chondrodysplasia punctata), central nervous system diseases (Marinesco-Sjogren syndrome, Walker Waarburg syndrome), intrauterine infections (Toxoplasmosis, rubella, cytomegalovirus, herpes simplex, varicella, syphilis), dermatologic diseases (ectodermal displasia, incontinentia pigmenti, Werner syndrome, ichthyosis, progeria), renal diseases (Lowe syndrome, Alport syndrome), muscular diseases (myotonic dystrophia, Walker Warburg syndrome), apical syndromes (Rubinstein Taybi syndrome, Bardet Biedl syndrome, oculodentodigital dysplasia), chromosomal diseases (Trisomy 21, trisomy 18, trisomy 13, 4p deletion syndrome, 5p syndrome) are systematic diseases which may cause cataract. In this case, these disorders were ruled out by laboratory evaluations and clinical finding.

Cataract is a medical condition which is treated surgically and progressive if not treated. There are a number of drugs besides systemic diseases which may cause cataract. For this reason, the administered drugs should be considered in an infant with congenital cataract. In this case, linezolid was initiated after VRE isolation in the blood culture, bilateral cataract was determined immediately on the second day of treatment, progression of cataract was observed during linezolid treatment and regression was achieved 2 days after the cessation of treatment, which disappeared totally in one week. In this case, progression of cataract under linezolid treatment and total regression after termination of medication suggests the reason of cataract was the side effect of linezolid. On the other hand, its mechanism of action remains unclear regarding development of cataract under linezolid treatment and total regression of cataract about a week after discontinuation of linezolid. To the authors’ knowledge, cataract development due to linezolid has not been reported yet.

In a meta-analysis of linezolid, the most common side effects are reported as diarrhea and nausea (%7, 8 - 9), headache (%6, 5) and vomiting (%2, 9 - 11, 0) followed by skin rashes and transient elevations of hepatic enzymes. Reversible myelosuppression rate is informed as %6.4. Meisner et al. reported frequency of thrombocytopenia as %1.4 in their study examining side effects of linezolid in children with gram positive bacterial infections. There are only a few studies about linezolid side effects and its reliability in newborns. Deville et al. studied 63 newborn patients with gram positive infections. Among these newborns, 43 of them were treated with linezolid and 20 with vancomycin as a choice of antibiotic. The group reported that sepsis recovery and side effects related with the medication was lower in the linezolid group. Moreover, they found out that decrease in hemoglobin levels and increase in bilirubin levels is higher in the linezolid group. It was also observed in this case that platelet count decreased during linezolid treatment and increased without transfusion 2 days after the cessation of treatment.

In conclusion, while linezolid treatment is beneficial in serious infections caused by resistant micro-organisms; it should be kept in mind that it may lead to cataract especially in preterm newborns and repeated ophthalmological examinations should be programmed.
Cataract in a preterm newborn

REFERENCES


